

Supplementary Material

Laprise JF, Markowitz LE, Chesson HW, et al. Comparing 2- and 3-dose 9-valent HPV vaccine schedules in the U.S.: A Cost-effectiveness analysis

Supplementary Figure 1. Vaccination strategies

Supplementary Figure 2. Vaccination coverage

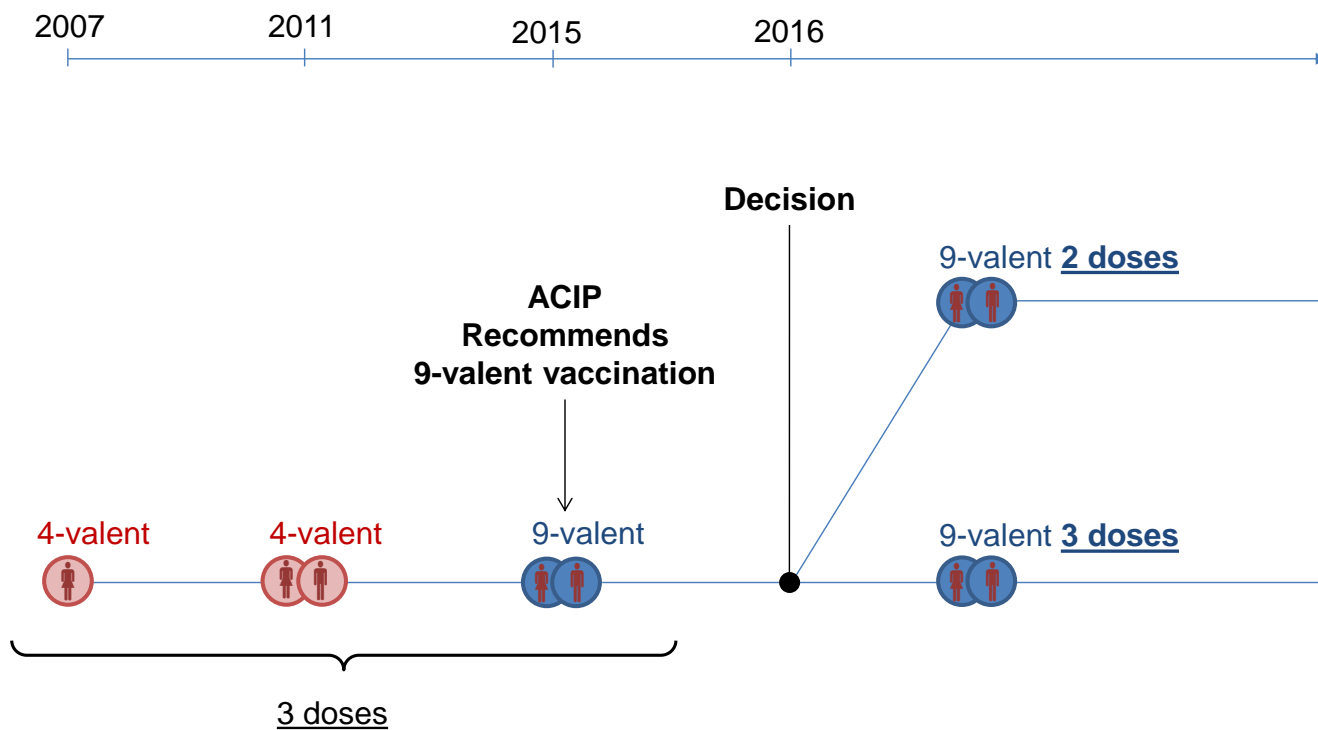
Supplementary Table 1. Economic parameters

Supplementary Table 2. Percentage point reduction in incidence 100 years after vaccination start

Supplementary Table 3. Sensitivity analysis - Incremental cost-effectiveness (\$/QALY-gained)

This supplementary material has been provided by the authors to give readers additional information about their work.

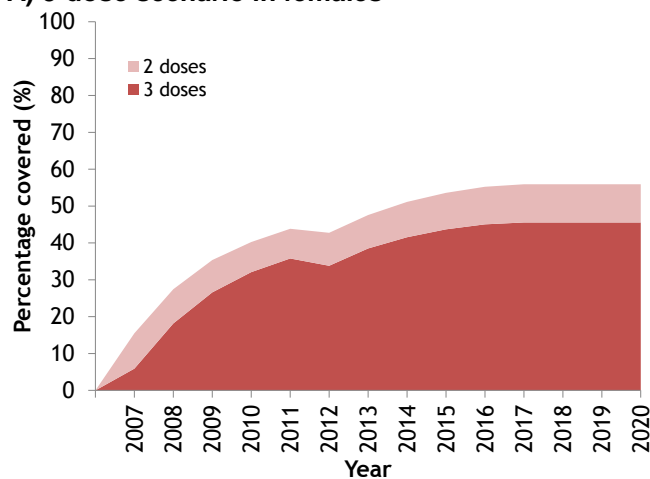
Supplementary Figure 1. Vaccination scenarios



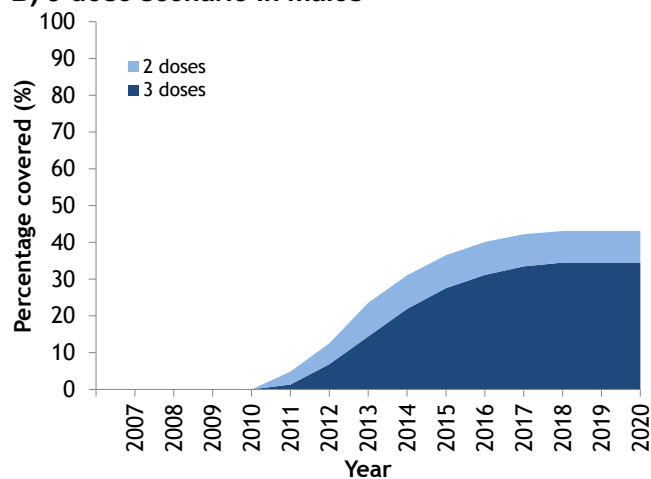
Two HPV vaccination scenarios were examined in the context of 9-valent HPV vaccination in the US: 1) continuing with 3-dose 9-valent vaccination, and 2) switching to 2-dose 9-valent vaccination. For the two scenarios, we modeled the changes in HPV vaccination in the United States from 2007 up to 2014 (i.e., introduction of gender-neutral vaccination in 2011). All changes to the current HPV vaccination strategy were modeled to occur at the beginning of 2016.

Supplementary Figure 2. Vaccination coverage (13-17 year-olds)

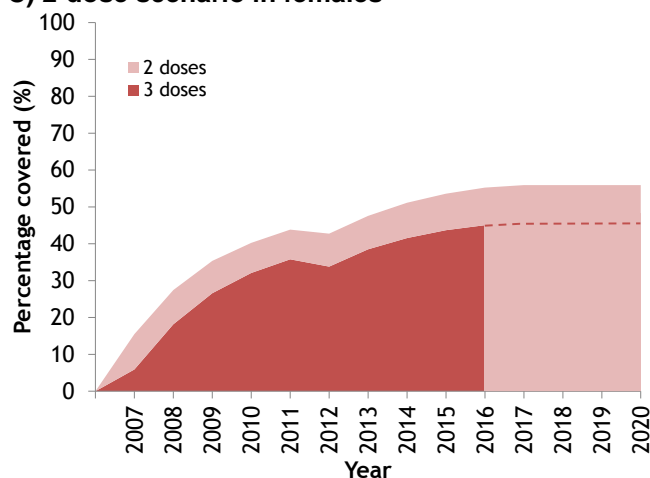
A) 3-dose scenario in females



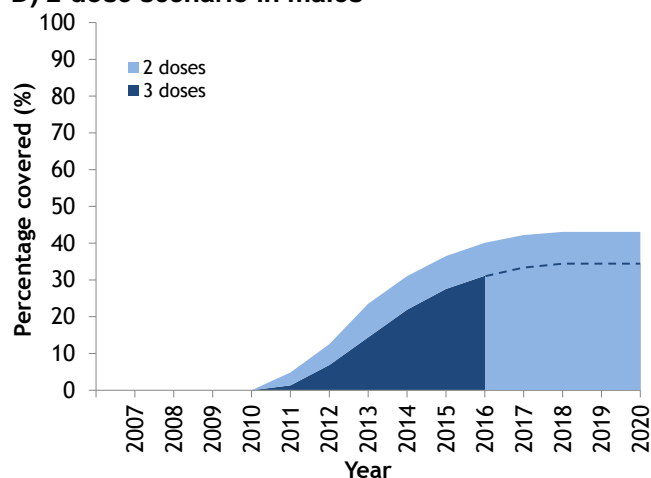
B) 3-dose scenario in males



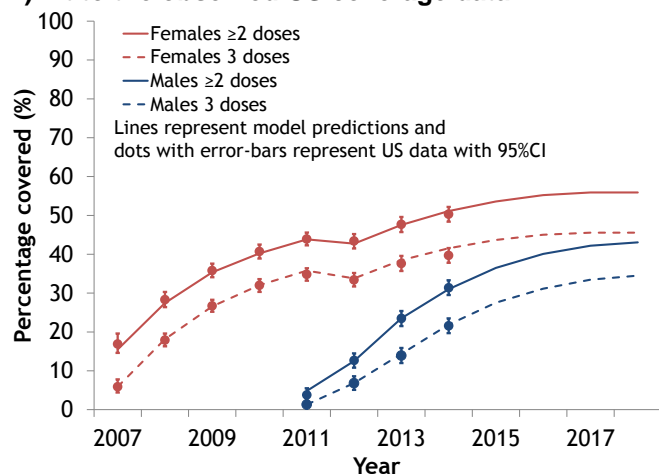
C) 2-dose scenario in females



D) 2-dose scenario in males



E) Fit to the observed US coverage data



Overall vaccination coverage in 13-17 year-olds for 2 and 3 doses.

A-D) Vaccination coverage for the 3-dose scenario in females (A) and males (B), and the 2-dose scenario in females (C) and males (D). Light- and dark-colored areas represent the proportion who will receive 2 and 3 doses, respectively. **E)** Fit to the observed US coverage data.

Supplementary Table 1. Economic parameters

	Reference scenario ^a	Sensitivity analysis		References
		Minimum	Maximum	
<u>Case-fatality^b</u>				
Cervical cancer (stage 1; 2-3; 4)	9%; 42%; 82%	8%; 31%; 80%	10%; 43%; 84%	[1]
Vulvar/vaginal	33%	31%	35%	[1]
Anal	31%	30%	32%	[1]
Oropharyngeal	39%	39%	40%	[1]
Penile	32%	29%	35%	[1]
% AGW attributed to HPV-6/11 ^c	90%	66%	100%	[2-5]
<u>AGW consultations per episode</u>				
Women	1.15	1.12	1.23	[6]
Men	1.21	1.15	1.33	[6]
<u>QALYs-lost</u>				
QALYs-lost per episode				
AGW	0.02	0.01	0.04	[7, 8]
CIN1 or LSIL	0.006	0.006	0.008	[9]
CIN2/3 or HSIL	0.01	0.009	0.012	[9]
Disutility				
Cervical cancer (stage 1; 2-3; 4)	28%;39%;45%	19%;29%;29%	51%;58%;64%	[10-12]
Vulvar/vaginal	32%			
Anal	51%			
Oropharyngeal	25%			
Penile	29%			
<u>Costs (\$US)</u>				
Dose of HPV vaccine ^d				
4-valent	145			[13]
9-valent	158			[13]
AGW episode				
Women	662	543	723	[14-16]
Men	866	543	1,021	[14-16]
Normal cytology	113	74	143	[17-19]
Colposcopy/biopsy	511	314	755	[18, 20]
CIN2/3 treatment ^e	2,712	1,644	4,269	[20-22]
Cervical cancer (stage 1; 2-3; 4)	34,332; 36,759; 58,878	15,386; 19,127; 20,654	35,775; 47,418; 132,935	[18, 20]
Relative costs vs. Cervical cancer (stage 1)				
Vulvar/vaginal	81%	67%	95%	[17]
Anal	115%	96%	135%	[17]
Oropharyngeal	138%	114%	161%	[17]
Penile	63%	52%	74%	[17]

ABBREVIATIONS: AGW: Anogenital warts; CIN: Cervical intraepithelial neoplasia; LSIL: Low-grade squamous intraepithelial lesion; QALY: Quality-adjusted life-years

^a Reference case values are the median from the literature

^b (Case fatality) = 100% – (5-year survival [%])

^c Proportion of HPV-6 and 11 among HPV positive anogenital warts

^d With \$15 vaccine administration cost

^e Treatment costs excluding the initial Pap and colposcopy/biopsy

All costs are \$US 2013.

Supplementary Table 2. Percentage point reduction in incidence 100 years after vaccination start

	Mean (80% UI)			
	Anogenital warts ^a	CIN2/3	Cervical cancer	All HPV-associated cancers
<u>2 doses</u>				
2-dose duration:				
Lifelong	86 (81; 90)	87 (80; 91)	87 (82; 91)	75 (72; 77)
30 years	81 (70; 90)	85 (78; 88)	86 (81; 90)	74 (71; 76)
25 years	75 (56; 90)	81 (74; 85)	83 (77; 88)	72 (69; 74)
20 years	68 (46; 89)	76 (68; 81)	78 (71; 83)	69 (65; 71)
15 years	53 (32; 80)	67 (56; 73)	70 (60; 76)	63 (56; 66)
10 years	30 (12; 48)	54 (38; 62)	58 (44; 65)	53 (42; 58)
<u>3 doses vs. 2 doses^b</u>				
2-dose duration:				
Lifelong	0 (0; 0)	0 (0; 0)	0 (0; 0)	0 (0; 0)
30 years	5 (0; 15)	2 (1; 3)	2 (0; 4)	1 (0; 2)
25 years	11 (0; 26)	5 (4; 6)	4 (2; 7)	3 (2; 4)
20 years	18 (1; 37)	11 (8; 13)	9 (6; 12)	6 (5; 8)
15 years	33 (10; 49)	19 (15; 25)	17 (13; 23)	12 (10; 16)
10 years	56 (42; 69)	33 (27; 42)	30 (24; 38)	22 (18; 30)
2-dose coverage (duration=20 years) ^c :				
5 pp increase	11 (0; 27)	7 (3; 10)	5 (2; 8)	3 (2; 5)
15 pp increase	0 (-3; 3)	3 (-1; 5)	-1 (-2; 4)	0 (-1; 1)

ABBREVIATIONS: UI: Uncertainty interval; CIN: Cervical intraepithelial neoplasia of grade 2 or 3; pp: percentage point.

REFERENCE CASE: Vaccine efficacy=95%, 3-dose duration of protection=Lifelong, time horizon=100 years

PREDICTIONS: Mean estimate generated by the 50 best fitting parameter sets. Each parameter set run 20 times. Uncertainty intervals (80%UI): 10th and 90th percentiles of model results based on the 50 best fitting parameter sets, reflects uncertainty in the natural history parameters.

^a We assume 90% of anogenital warts are due to HPV-6/11

^b Additional reduction provided by the 3rd dose compared to 2 doses. We assume 3 doses confer lifelong protection

^c We assume 2 and 3 doses confer 20-year and lifelong protection, respectively. A negative number indicates that the 2-dose strategy (with increased coverage) provides a larger reduction than the 3-dose strategy.

Supplementary Table 3. Sensitivity analysis - Incremental cost-effectiveness (\$/QALY-gained)

2-dose duration of protection	Mean (80%UI)			
	2 doses (vs. No vaccination)		3 rd dose ^a (vs. 2 doses)	
	20 years	Lifelong	20 years	Lifelong
Reference scenario	CS (CS; 1,500)	CS (CS; 500)	118,700 (57,000; 307,500)	Dominated
2-dose efficacy=85% & duration=Lifelong	n/a	CS (CS; 1,000)	n/a	144,800 (82,600; 429,800)
Screening Program Co-testing ^b	CS (-; -)	CS (-; -)	96,500 (48,800; 206,900)	Dominated
Increase in 2-dose coverage:				
5% increase ^c			Dominated (167,400; Dominated)	Dominated
15% increase ^c			Dominated (Dominated; Dominated)	Dominated
Economic parameters				
Minimum disease burden ^d	CS (CS; 2,900)	CS (CS; 1,900)	141,700 (70,500; 393,300)	Dominated
Maximum disease burden ^d	CS (CS; 900)	CS (CS; 100)	53,000 (23,600; 159,700)	Dominated
Minimum healthcare costs ^d	5,800 (3,700; 8,200)	4,800 (3,300; 7,200)	122,600 (63,300; 325,800)	Dominated
Maximum healthcare costs ^d	CS (CS; CS)	CS (CS; CS)	109,200 (51,400; 291,700)	Dominated
Time horizon=30 years	9,400 (3,600; 18,300)	9,100 (3,900; 17,700)	Dominated (119,800; Dominated)	Dominated
Discount=5%/year	3,500 (CS; 9,300)	2,600 (CS; 8,000)	305,900 (106,500; >1million)	Dominated

ABBREVIATIONS: QALY: Quality-Adjusted Life-Year; UI: Uncertainty interval; CS: Cost-saving; UI: Uncertainty interval
REFERENCE CASE: Vaccine efficacy=95%, 3-dose duration of protection=Lifelong, Vaccine cost/dose=\$158 (with administration fees),
Time horizon=100 years

PREDICTIONS: Mean estimate generated by the 50 best fitting parameter sets. Each parameter set run 20 times. Uncertainty intervals
(80%UI): 10th and 90th percentiles of model results based on the 50 best fitting parameter sets, reflects uncertainty in the natural history
parameters.

^a We assume 3 doses confer lifelong protection.

^b Co-testing: 21-29 year-olds have a cytology test every 3 years, and 30-65 year-olds have cytology/HPV DNA co-testing every 5 years.

^c Increase in coverage: Absolute increase in coverage for 2-dose vaccination

^d Minimum/Maximum: All cancer costs or QALY-lost parameters are set at the minimum/maximum value identified from the United States
literature(see Supplementary Table 1).

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